

Application No.: 08/487,312

Docket No.: 220002016004

REMARKS

New claims are proposed for the purpose of clarifying that included in the invention is the embodiment wherein the bGH sequences set forth at positions 2-191 of Figure 1 or 1-191 of Figure 1 or their allelic variants are preceded by a methionine codon. The addition of the sequence of positions 1-191 of Figure 1 to claim 19 is done only in order to provide antecedent basis for proposed new claims 23, 26, 28 and 30, and their dependent claims. This amendment is clearly supported in Figure 1 itself and on page 15 of the specification, lines 6-9.

Support for expression of bovine growth hormone with an N-terminal methionine is supported in the specification, for example, on page 9, last full paragraph which states that growth hormone can be expressed directly by following the procedure described in Goeddel, D. V., *et al.*, *Nature* (1979) 281:544. In the procedure of Goeddel (copy enclosed) Met-preceded human growth hormone sequence is obtained. Although retention of methionine is not determined in this article, this is verified by the enclosed U.S. patent 4,658,021. The '021 patent describes the same experiment as the article (pHGH 107 in *E. coli*).

Support for claims where RNA is obtained with the start codon (encoding methionine) is found in that paragraph as well; although the paragraph states that the start codon AUG can be blunt end-ligated to the "cDNA" coding for growth hormone. It is understood that AUG refers to RNA which will in turn be translated into the desired protein. The position of AUG as located in RNA when translation occurs is further described on page 8, approximately 10 lines from the bottom.

Proposed claim 32 (which requires expression in bacteria) is supported, for example, on page 6, line 3. Support for expression in *E. coli* is supported in original claim 21 and in the examples.

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Thus, no new matter has been added and entry of the amendment is respectfully requested. The amendment is made, as set forth above, to clarify that direct expression occurs by inserting a codon encoding methionine before the N-terminus of the bovine growth hormone sequences presented in the application.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 220002016004.

Respectfully submitted,

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